



B<sup>1</sup>  
cont

Figure 1B shows the amino acid sequence connecting the carboxyl terminus of the L chain and the amino terminus of the H chain and an engineered loop region containing an enterokinase cleavage site. The amino acid sequence of the upstream untranslated region is indicated as SEQ ID NO: 19.—

Please replace the paragraph on page 14, lines 8-11 with the following:

B<sup>2</sup>

--Figure 5 is a depiction of the peptide fragments generated upon incubation of the recombinant single-chain TeTx with trypsin and Arg C protease, and deduction, from the N-terminal sequences of one of the resulting fragments (SEQ ID NO: 20) of the amino acid sequence recognized by these agents. --

Please replace the paragraph on page 14, lines 22-24 with the following:

Please replace the paragraph on page 14, lines 8-11 with the following:

--Figure 5 is a depiction of the peptide fragments generated upon incubation of the recombinant single-chain TeTx with trypsin and Arg C protease, and deduction, from the N-terminal sequences of one of the resulting fragments (SEQ ID NO: 20) of the amino acid sequence recognized by these agents. --

Please replace the paragraph on page 14, lines 22-24 with the following:

B<sup>3</sup>

--Figure 10 shows the scheme for construction of a plasmid encoding single-chain BoNT/E, and an agarose gel electrophoretogram of the PCR fragment (SEQ ID NO: 21) obtained during the construction of the plasmid, along with the deduced amino acid sequence of the fragment (SEQ ID NO: 24).—

Please replace the paragraph beginning on page 9, line 19 of the specification with the following paragraph.

B<sup>4</sup>  
--To reduce the risk of unintentional activation of the toxin by human or commonly encountered proteases, the amino acid sequences of the cleavage site are preferably designed to have a high degree of specificity to proteolytic enzymes which do not normally occur in humans (as either human proteases or occurring in part of the foreseeable human fauna and flora). A non-exclusive list of examples of such proteases includes bovine enterokinase, which cleaves the amino acid sequence DDDDK (SEQ ID NO: 15); tobacco etch virus (TEV) protease, which cleaves the sequences EXXYXQS (SEQ ID NO: 22) AND EXXYQG (SEQ ID NO 23); GENENASE<sup>®</sup> from *Bacillus amyliquisfaciens*, which cleaves the sequence HY or YH; and PRESSION<sup>®</sup> protease from human rhinovirus 3C, which cleaves the amino acid sequence LEVLFQGP (SEQ ID NO: 16). As used above, the letter X indicates any amino acid. All amino acid sequences shown in the present specification are in the direction from amino terminus to carboxyl terminus, and all nucleotide sequences from 5' to 3', (from left to right) unless otherwise indicated.—

Please replace the paragraph beginning on page 30, line 11 of the specification with the following paragraph.

B<sup>5</sup>  
-- The resulting plasmid construct contains the nucleotide sequence encoding the single-chain toxin protein, comprising (from amino to carboxyl terminus): six histidine residues (the His tag), followed by the L chain, an enterokinase cleavage site, and the H chain. The translated junction between the L and H chains containing the EK cleavage site (DDDDK) (SEQ ID NO: 15) is shown below (in the direction from N-terminus to C-terminus) and in Figure 1.--